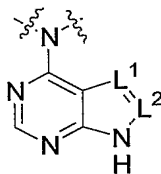


Claims

We claim:

1. A compound comprising one or more phosphonates and a substructure of formula I:



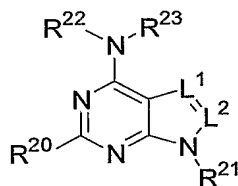
I

wherein L^1 and L^2 are -N- or -CR^a-; and

R^a is hydrogen, alkyl, substituted alkyl, aryl or substituted aryl;

or a pharmaceutically acceptable salt thereof.

2. The compound of claim 1 that comprises a substructure of the formula:



wherein:

L^1 and L^2 are independently -N-, or -CR^a-, provided that only one of L^1 or L^2 is a nitrogen atom;

R^a is hydrogen, alkyl, aryl or substituted aryl;

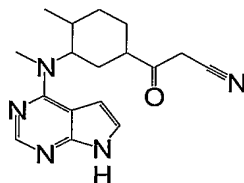
R²⁰ is hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl aryl, cycloalkyl, substituted aryl, or -NR^bR^c;

R^b and R^c are independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, or aralkyl;

R²¹ is hydrogen, alkyl, cycloalkyl, substituted cycloalkyl, substituted alkyl, aryl, substituted aryl, aralkyl, or substituted aralkyl; and

R^{22} and R^{23} are independently hydrogen, alkyl, substituted aryl, or aralkyl.

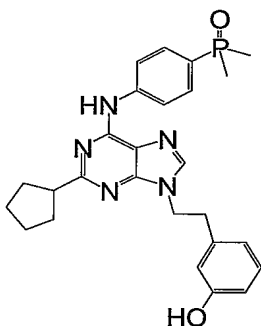
3. The compound of claim 1 that comprises a substructure of formula II:



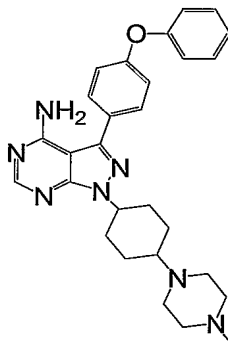
5

II

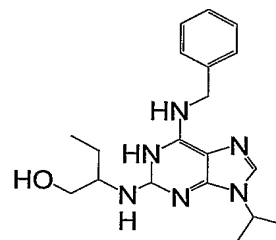
4. The compound of claim 1 that comprises a substructure of formula IIIa, IVa or Va:



IIIa

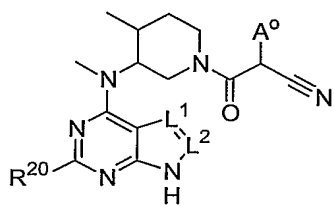


IVa

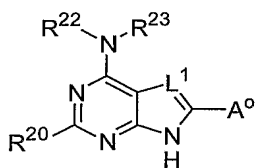


Va

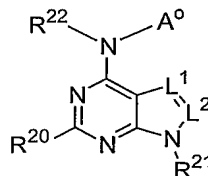
10 5. The compound of claim 1 having formula 1, 2, 3, or 4:



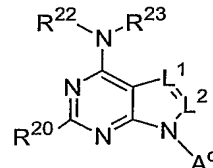
1



2



3



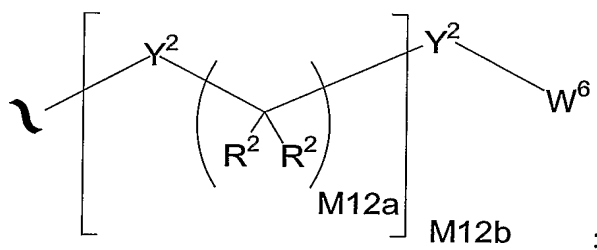
4

wherein:

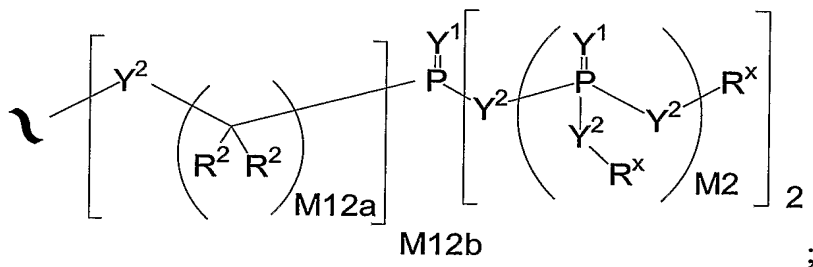
A^0 is A^1 ;

15

A^1 is:



A³ is:



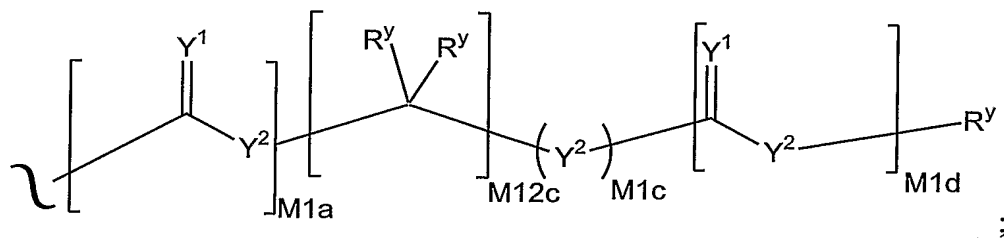
5

Y¹ is independently O, S, N(R^x), N(OR^x), or N(N(R^x)(R^x));

Y² is independently a bond, O, N(R^x), N(OR^x), N(N(R^x)(R^x)), or -S(O)_{M2}-; and when Y² joins two phosphorous atoms Y² can also be C(R²)(R²);

10

R^x is independently H, R², W³, a protecting group, or the formula:



R^y is independently H, W³, R² or a protecting group;

15 R² is independently H, R³ or R⁴ wherein each R⁴ is independently substituted with 0 to 3 R³ groups;

R³ is R^{3a}, R^{3b}, R^{3c} or R^{3d}, provided that when R³ is bound to a heteroatom, then R³ is R^{3c} or R^{3d};

R^{3a} is F, Cl, Br, I, -CN, N₃ or -NO₂;

R^{3b} is Y¹;

R^{3c} is $-R^x$, $-N(R^x)(R^x)$, $-SR^x$, $-S(O)R^x$, $-S(O)_2R^x$, $-S(O)(OR^x)$, $-S(O)_2(OR^x)$, $-OC(Y^1)R^x$, $-OC(Y^1)OR^x$, $-OC(Y^1)(N(R^x)(R^x))$, $-SC(Y^1)R^x$, $-SC(Y^1)OR^x$, $-SC(Y^1)(N(R^x)(R^x))$, $-N(R^x)C(Y^1)R^x$, $-N(R^x)C(Y^1)OR^x$, or $-N(R^x)C(Y^1)(N(R^x)(R^x))$;

5 R^{3d} is $-C(Y^1)R^x$, $-C(Y^1)OR^x$ or $-C(Y^1)(N(R^x)(R^x))$;

R^4 is an alkyl of 1 to 18 carbon atoms, alkenyl of 2 to 18 carbon atoms, or alkynyl of 2 to 18 carbon atoms;

R^5 is R^4 wherein each R^4 is substituted with 0 to 3 R^3 groups;

W^3 is W^4 or W^5 ;

10 W^4 is R^5 , $-C(Y^1)R^5$, $-C(Y^1)W^5$, $-SO_2R^5$, or $-SO_2W^5$;

W^5 is carbocycle or heterocycle wherein W^5 is independently substituted with 0 to 3 R^2 groups;

W^6 is W^3 independently substituted with 1, 2, or 3 A^3 groups;

$M2$ is 0, 1 or 2;

15 $M12a$ is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12;

$M12b$ is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12;

$M1a$, $M1c$, and $M1d$ are independently 0 or 1;

$M12c$ is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12;

20 L^1 and L^2 are independently $-N-$, or $-CR^a-$, provided that only one of L^1 or L^2 is a nitrogen atom;

R^a is hydrogen, alkyl, aryl or substituted aryl;

R^{20} is hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl aryl, cycloalkyl, substituted aryl, or $-NR^bR^c$;

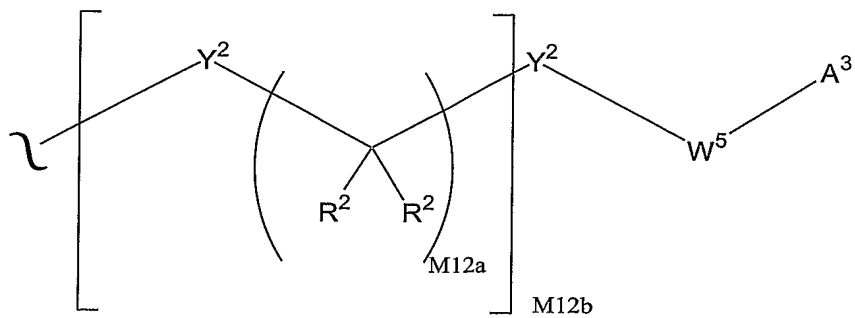
25 R^b and R^c are independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, or aralkyl;

R^{21} is hydrogen, alkyl, cycloalkyl, substituted cycloalkyl, substituted alkyl, aryl, substituted aryl, aralkyl, or substituted aralkyl; and

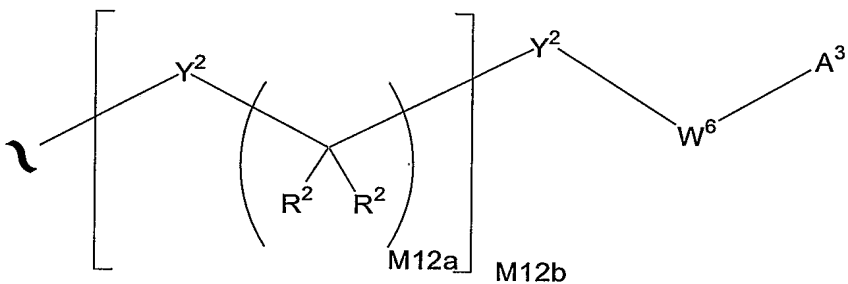
R^{22} and R^{23} are independently hydrogen, alkyl, substituted aryl, or aralkyl.

30

6. The compound of claim 5 wherein A^1 is of the formula:

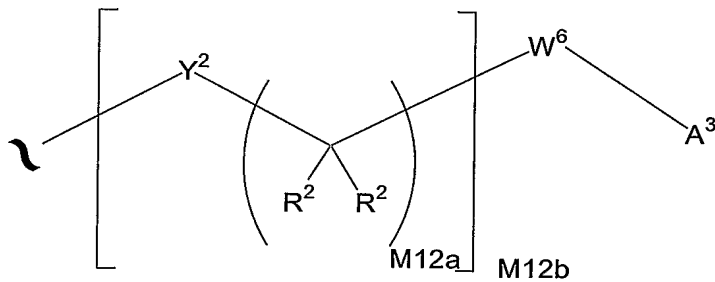


7. The compound of claim 5 wherein A¹ is of the formula:

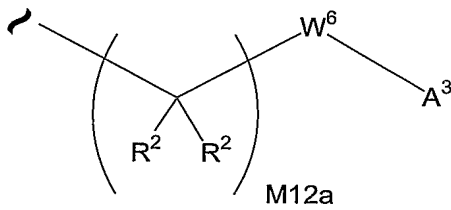


5

8. The compound of claim 5 wherein A¹ is of the formula:

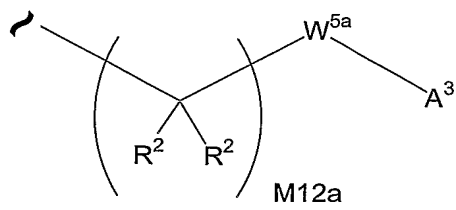


9. The compound of claim 5 wherein A¹ is of the formula:



10

10. The compound of claim 5 wherein A¹ is of the formula:

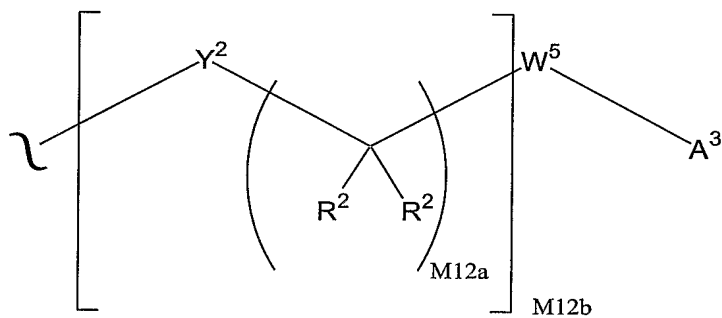


and W^{5a} is a carbocycle or a heterocycle where W^{5a} is independently substituted with 0 or 1 R^2 groups.

5

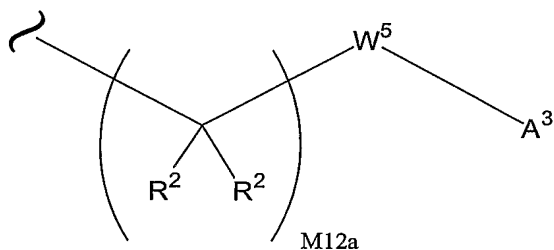
11. The compound of claim 5 wherein M12a is 1.

12. The compound of claim 5 wherein A^1 is of the formula:

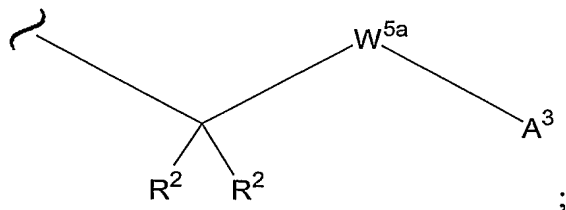


10

13. The compound of claim 5 wherein A^1 is of the formula:



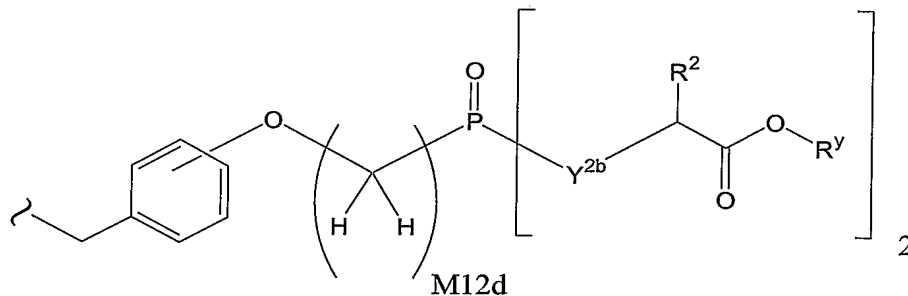
14. The compound of claim 5 wherein A^1 is of the formula:



15

W^{5a} is a carbocycle independently substituted with 0 or 1 R^2 groups;

15. The compound of claim 5 wherein A^1 is of the formula:



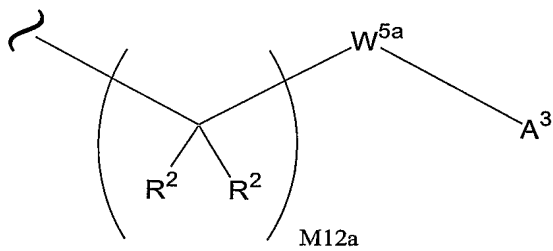
5

Y^{2b} is O or $N(R^2)$; and

M12d is 1, 2, 3, 4, 5, 6, 7 or 8.

16. The compound of claim 5 wherein A^1 is of the formula:

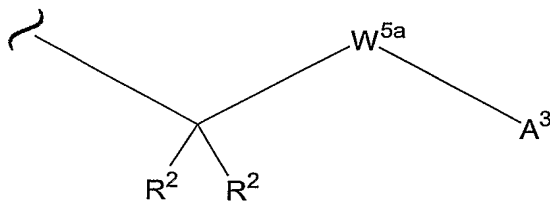
10



W^{5a} is a carbocycle independently substituted with 0 or 1 R^2 groups;

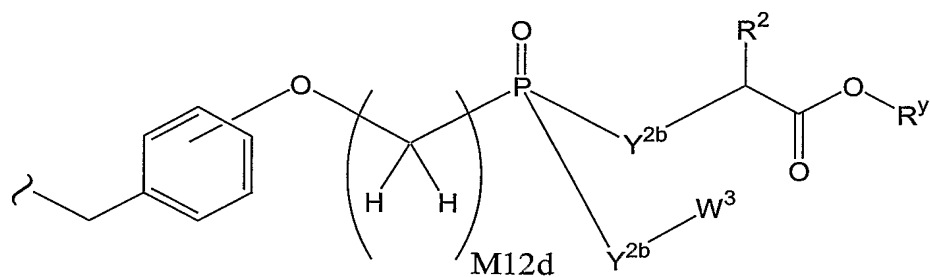
17. The compound of claim 5 wherein A^1 is of the formula:

15



W^{5a} is a carbocycle or heterocycle where W^{5a} is independently substituted with 0 or 1 R^2 groups.

- 20 18. The compound of claim 5 wherein A^1 is of the formula:

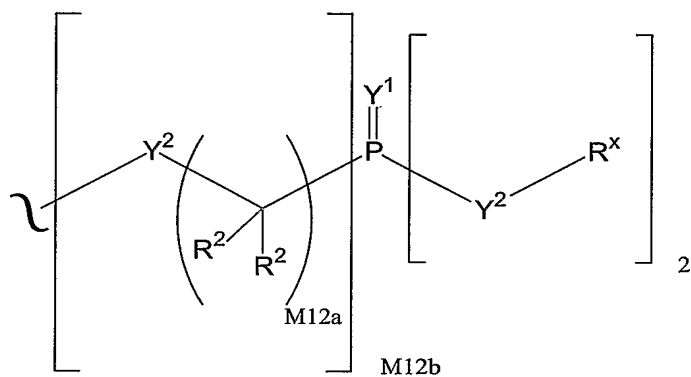


Y^{2b} is O or $N(R^2)$; and

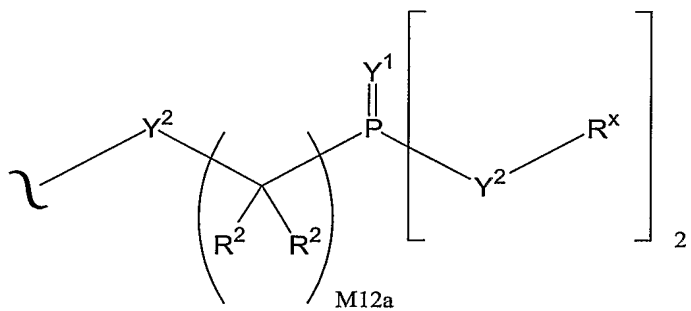
M12d is 1, 2, 3, 4, 5, 6, 7 or 8.

5

19. The compound of any one of claims 5-18 wherein A^3 is of the formula:

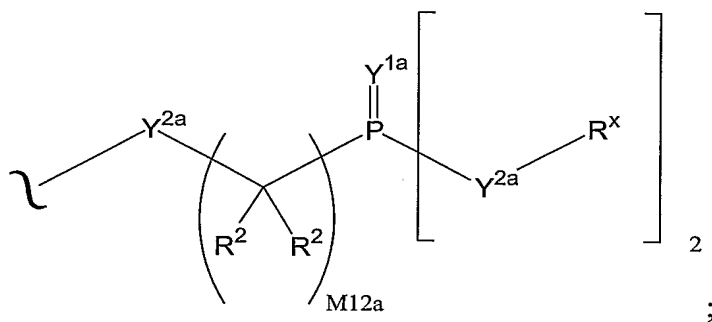


20. The compound of any one of claims 5-18 wherein A^3 is of the formula:



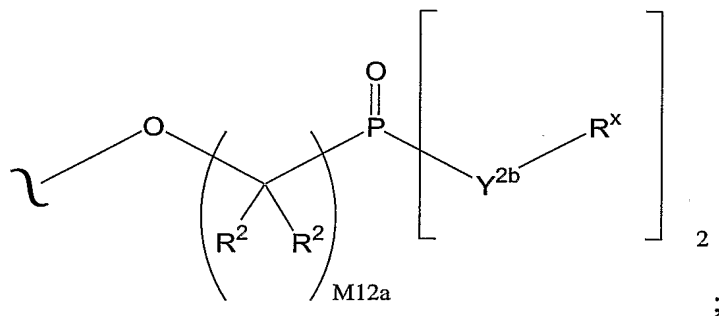
10

21. The compound of any one of claims 5-18 wherein A^3 is of the formula:



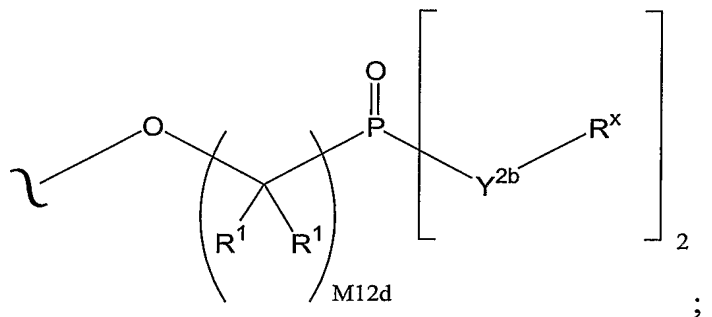
Y^{1a} is O or S; and
 Y^{2a} is O, $N(R^x)$ or S.

- 5 22. The compound of any one of claims 5-18 wherein A^3 is of the formula:



and Y^{2b} is O or $N(R^x)$.

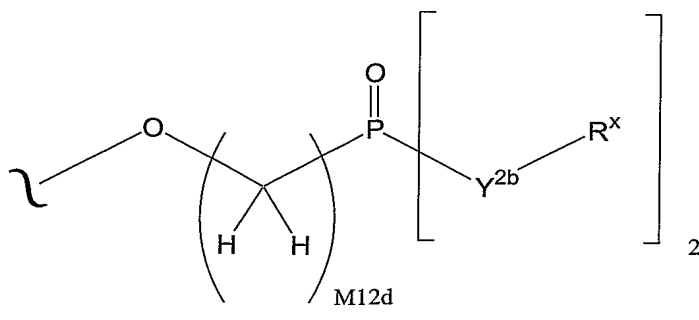
23. The compound of any one of claims 5-18 wherein A^3 is of the formula:



10

R^1 is independently H or alkyl of 1 to 18 carbon atoms;
 Y^{2b} is O or $N(R^x)$; and
M12d is 1, 2, 3, 4, 5, 6, 7 or 8.

- 15 24. The compound of any one of claims 5-18 wherein A^3 is of the formula:

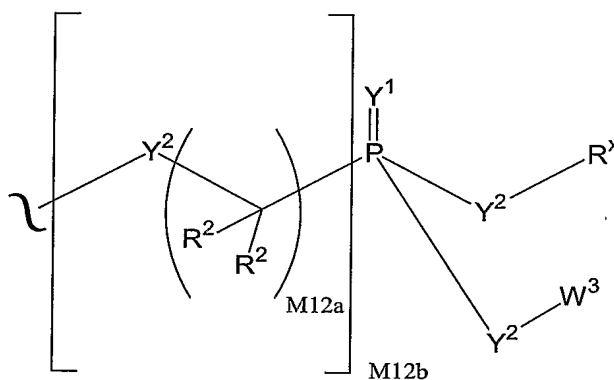


Y^{2b} is O or $N(R^x)$; and

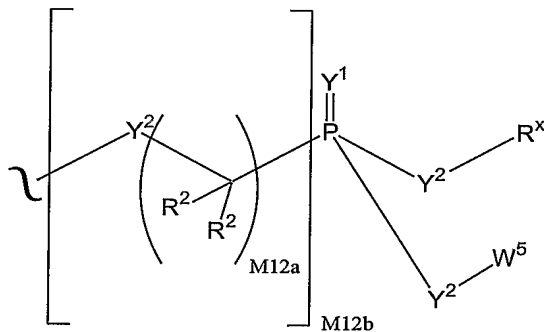
M12d is 1, 2, 3, 4, 5, 6, 7 or 8.

5 25. The compound of claim 24 wherein M12d is 1.

26. The compound of any one of claims 5-18 wherein A^3 is of the formula:

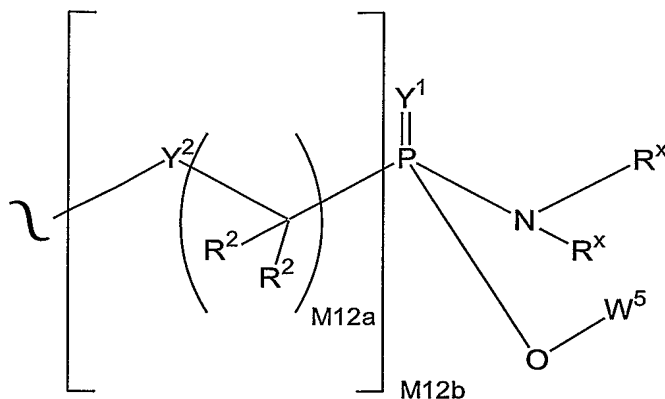


10 27. The compound of any one of claims 5-18 wherein A^3 is of the formula:



28. The compound of claim 27 wherein W^5 is a carbocycle.

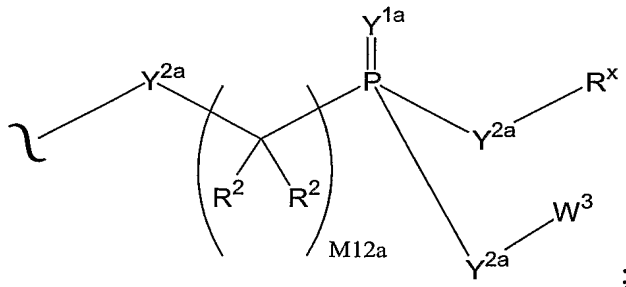
29. The compound of any one of claims 5-18 wherein A^3 is of the formula:



- 5 30. The compound of claim 29 wherein W^5 is phenyl.

31. The compound of claim 30 wherein M12b is 1.

32. The compound of any one of claims 5-18 wherein A^3 is of the formula:

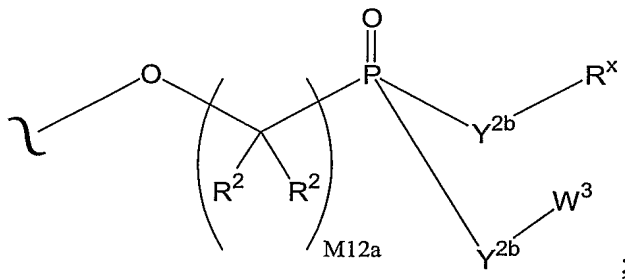


10

Y^{1a} is O or S; and

Y^{2a} is O, $N(R^x)$ or S.

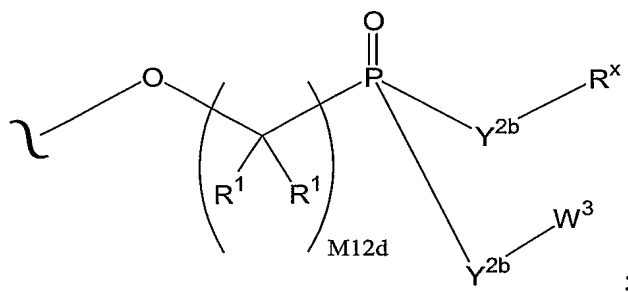
33. The compound of any one of claims 5-18 wherein A^3 is of the formula:



15

and Y^{2b} is O or $N(R^x)$.

34. The compound of any one of claims 5-18 wherein A^3 is of the formula:



R^1 is independently H or alkyl of 1 to 18 carbon atoms;

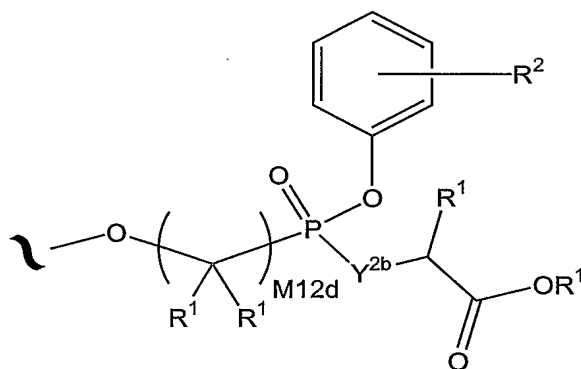
5 Y^{2b} is O or $N(R^x)$; and

M12d is 1, 2, 3, 4, 5, 6, 7 or 8.

35. The compound of claim 34 wherein R^1 is H.

- 10 36. The compound of claim 34 wherein M12d is 1.

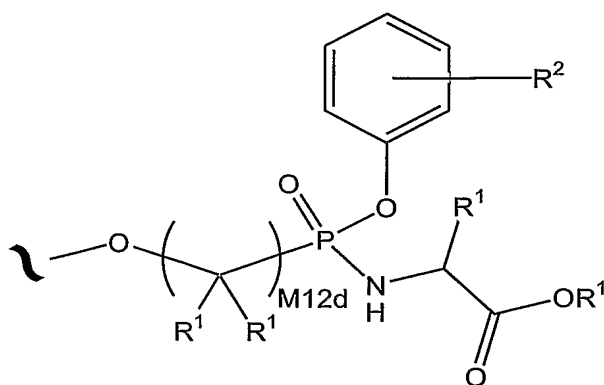
37. The compound of any one of claims 5-18 wherein A^3 is of the formula:



wherein the phenyl carbocycle is substituted with 0, 1, 2, or 3 R^2 groups.

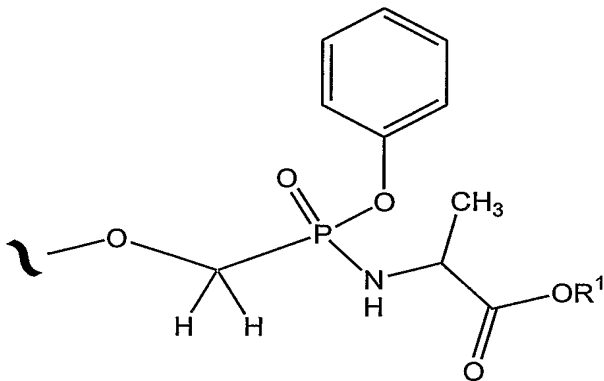
15

38. The compound of any one of claims 5-18 wherein A^3 is of the formula:



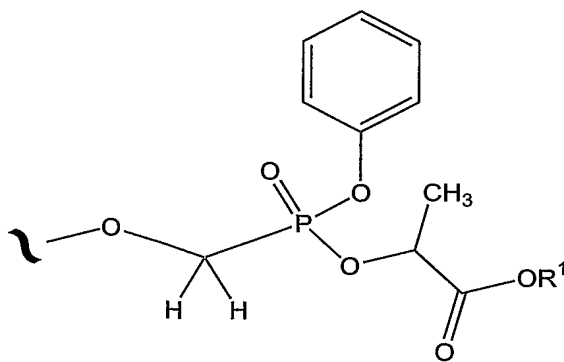
wherein R¹ is independently H or alkyl of 1 to 18 carbon atoms.

39. The compound of any one of claims 5-18 wherein A³ is of the formula:

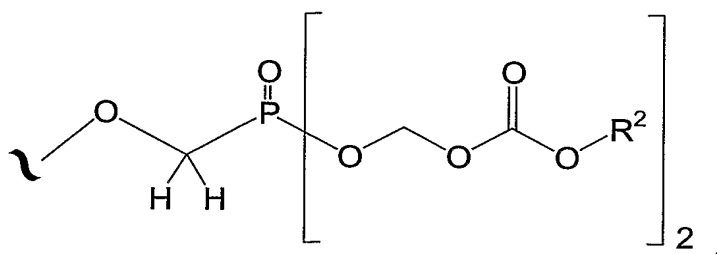


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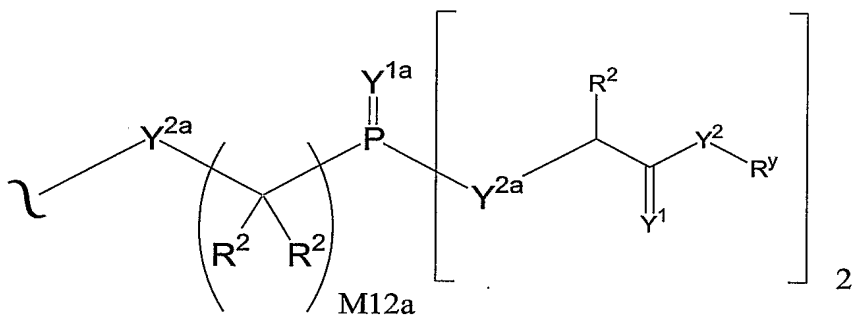
40. The compound of any one of claims 5-18 wherein A³ is of the formula:



10 41. The compound of any one of claims 5-18 wherein A³ is of the formula:



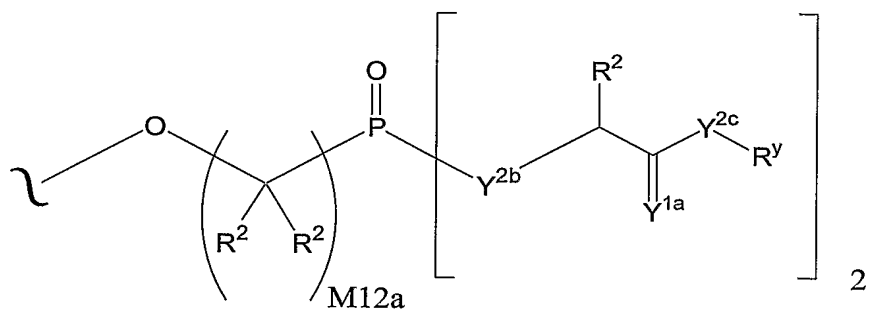
42. The compound of any one of claims 5-18 wherein A^3 is of the formula:



5

Y^{1a} is O or S; and
 Y^{2a} is O, $\text{N}(\text{R}^2)$ or S.

43. The compound of any one of claims 5-18 wherein A^3 is of the formula:

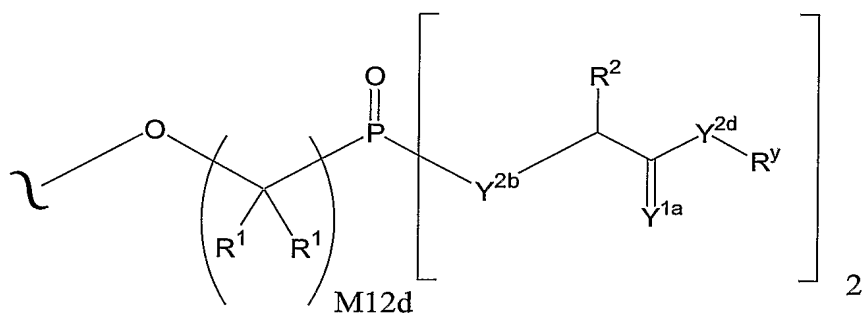


10

Y^{1a} is O or S;
 Y^{2b} is O or $\text{N}(\text{R}^2)$; and
 Y^{2c} is O, $\text{N}(\text{R}^y)$ or S.

15

44. The compound of any one of claims 5-18 wherein A^3 is of the formula:



R^1 is independently H or alkyl of 1 to 18 carbon atoms;

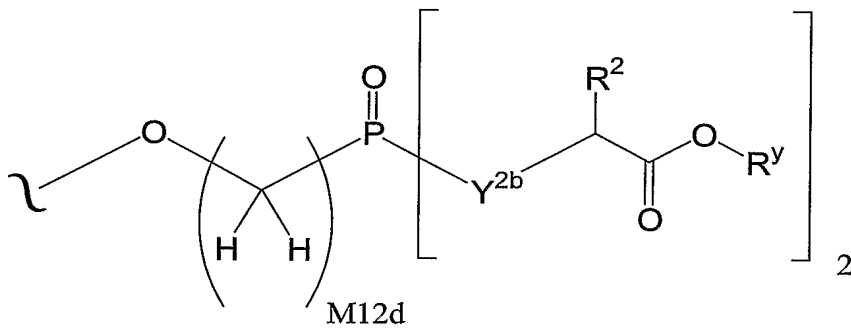
Y^{1a} is O or S;

Y^{2b} is O or N(R^2);

5 Y^{2d} is O or N(R^y); and

M12d is 1, 2, 3, 4, 5, 6, 7 or 8.

45. The compound of any one of claims 5-18 wherein A^3 is of the formula:

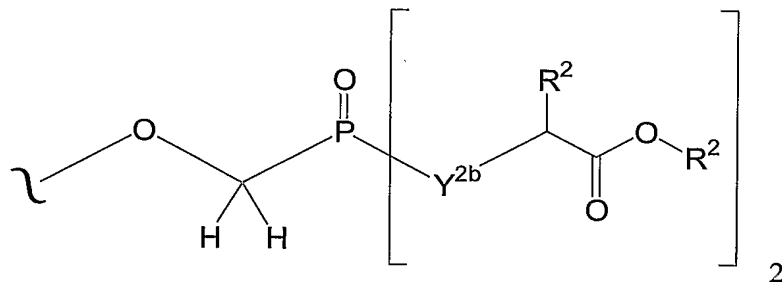


10

Y^{2b} is O or N(R^2); and

M12d is 1, 2, 3, 4, 5, 6, 7 or 8.

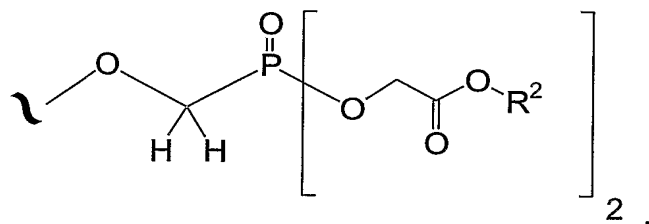
46. The compound of any one of claims 5-18 wherein A^3 is of the formula:



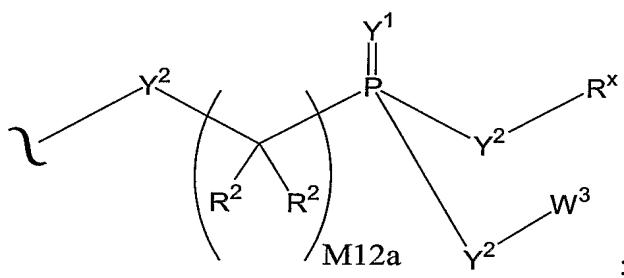
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and Y^{2b} is O or N(R^2).

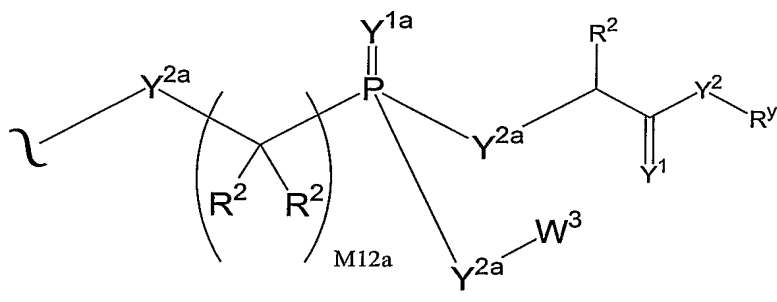
47. The compound of any one of claims 5-18 wherein A³ is of the formula:



- 5 48. The compound of any one of claims 5-18 wherein A³ is of the formula:



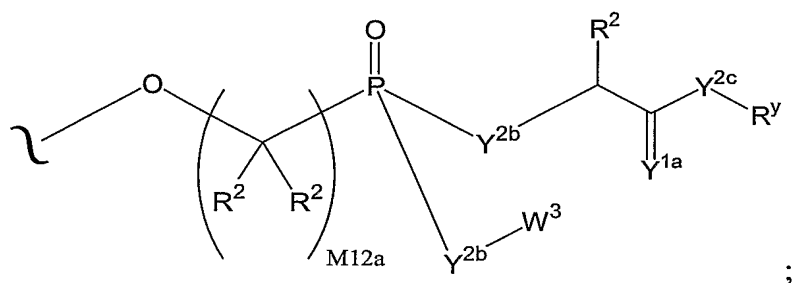
49. The compound of any one of claims 5-18 wherein A³ is of the formula:



Y^{1a} is O or S; and

Y^{2a} is O, N(R²) or S.

50. The compound of any one of claims 5-18 wherein A³ is of the formula:



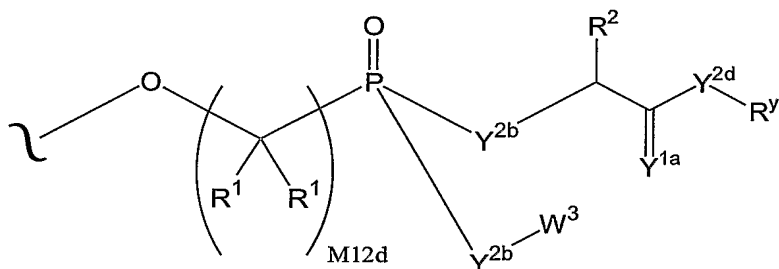
Y^{1a} is O or S;

Y^{2b} is O or $N(R^2)$; and

Y^{2c} is O, $N(R^y)$ or S.

5

51. The compound of any one of claims 5-18 wherein A^3 is of the formula:



R^1 is independently H or alkyl of 1 to 18 carbon atoms;

Y^{1a} is O or S;

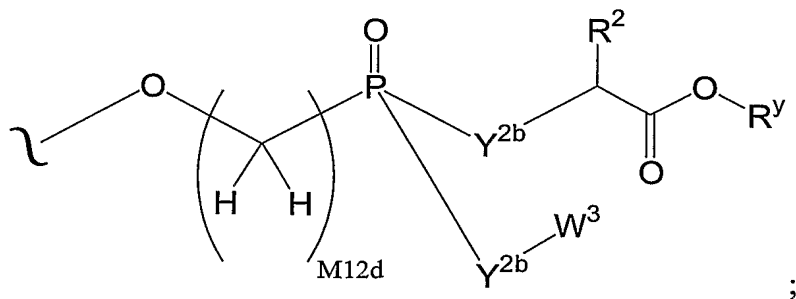
Y^{2b} is O or $N(R^2)$;

Y^{2d} is O or $N(R^y)$; and

M12d is 1, 2, 3, 4, 5, 6, 7 or 8.

10

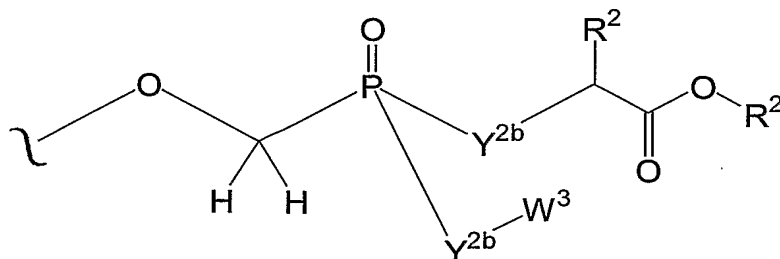
15 52. The compound of any one of claims 5-18 wherein A^3 is of the formula:



Y^{2b} is O or $N(R^2)$; and

M12d is 1, 2, 3, 4, 5, 6, 7 or 8.

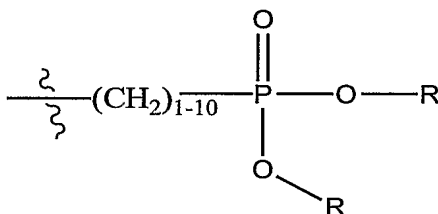
53. The compound of any one of claims 5-18 wherein A³ is of the formula:



and Y^{2b} is O or N(R²).

5

54. The compound of claim 5 wherein A⁰ is of the formula:



wherein each R is independently (C₁-C₆)alkyl.

10

55. The compound of claim 2 wherein:

R^a is hydrogen, or substituted aryl;

R²⁰ is hydrogen, cycloalkyl, or -NR^bR^c;

R^b is hydrogen, and R^c is substituted alkyl, or substituted aryl;

15 R²¹ is hydrogen, alkyl, substituted cycloalkyl, or substituted aralkyl;

R²² is hydrogen, or alkyl; and

R²³ is hydrogen, substituted aryl, substituted cycloalkyl, or aralkyl.

56. The compound of any one of claims 1-55 which inhibits a
 20 serine/threonine kinase, tyrosine kinase, Bcr-Abl kinase, cyclin-dependent kinase, Flt3 tyrosine kinase, MAP Erk kinase, JAK3 kinase, VEGF receptor kinase, PDGF receptor tyrosine kinase, protein kinase C, insulin receptor tyrosine kinase, and/or an EGF receptor tyrosine kinase.

57. A pharmaceutical composition comprising a pharmaceutically acceptable excipient and a compound as described in any one of claims 1-55.
58. A unit dosage form comprising a compound as described in any one of
5 claims 1-55 and a pharmaceutically acceptable excipient.
59. A method for inhibiting a kinase *in vitro* or *in vivo* comprising contacting a sample in need of such treatment with a compound as described in any one of claims 1-55.
- 10 60. The method of claim 59 wherein the contacting is *in vivo*.
61. A method of inhibiting a kinase in an animal, comprising administering a compound as described in any one of claims 1-55 to the animal.
- 15 62. The method of claim 61 wherein the compound is formulated with a pharmaceutically acceptable carrier.
63. The method of claim 62 wherein the formulation further comprises a
20 second active ingredient.
64. The method of any one of claims 59-63 wherein the kinase is a serine/threonine kinase, tyrosine kinase, Bcr-Abl kinase, cyclin-dependent kinase, Flt3 tyrosine kinase, MAP Erk kinase, JAK3 kinase, VEGF receptor
25 kinase, PDGF receptor tyrosine kinase, protein kinase C, insulin receptor tyrosine kinase, and/or an EGF receptor tyrosine kinase.
65. A method of treating cancer in an animal in need of such treatment comprising administering an effective amount of a compound as described in
30 any one of claims 1-55 to the animal.

66. A compound as described in any one of claims 1-55 for use in medical therapy.
67. The use of a compound as described in any one of claims 1-55 to prepare
5 a medicament for inhibiting a kinase in an animal.
68. The use of claim 67 wherein the kinase is a serine/threonine kinase, tyrosine kinase, Bcr-Abl kinase, cyclin-dependent kinase, Flt3 tyrosine kinase, MAP Erk kinase, JAK3 kinase, VEGF receptor kinase, PDGF receptor tyrosine
10 kinase, protein kinase C, insulin receptor tyrosine kinase, and/or an EGF receptor tyrosine kinase.
69. The use of a compound as described in any one of claims 1-55 to prepare a medicament for treating cancer in an animal.
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70. A method for preparing a compound as described in the schemes and examples herein.
71. A method for preparing a pharmaceutical composition, comprising
20 combining a pharmaceutically acceptable excipient and a compound as described in any one of claims 1-55.